

General

Guideline Title

Congress of Neurological Surgeons systematic review and evidence-based guideline on surgical techniques and technologies for the management of patients with nonfunctioning pituitary adenomas.

Bibliographic Source(s)

Kuo JS, Barkhoudarian G, Farrell CJ, Bodach ME, Tumialan LM, Oyesiku NM, Litvack Z, Zada G, Patil CG, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on surgical techniques and technologies for the management of patients with nonfunctioning pituitary adenomas. *Neurosurgery*. 2016 Oct;79(4):E536-8. [44 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The rating schemes used for the strength of the evidence (Class I-III) and the levels of recommendations (Level I-III) are defined at the end of the "Major Recommendations" field.

Note: The following questions address the role of technical aspects (adjuvants) of operative treatment of patients with nonfunctioning pituitary adenomas (NFPAs). These recommendations apply to initial operative treatment of adult patients with NFPAs.

Question

Do transsphenoidal or endoscopic surgical approaches lead to symptomatic relief for NFPA patients?

Level III Recommendation

Transsphenoidal microsurgery or endoscopic resection is recommended for symptomatic relief of nonfunctioning pituitary adenoma patients.

Question

What surgical approach is recommended for elderly NFPA patients?

Level III Recommendation

The transsphenoidal approach is recommended for NFPA resection in American Society of Anaesthesiologists (ASA) grade 1-3 elderly patients.

Question

Does bony exposure alter the extent of NFPA resection?

Level III Recommendation

Adequate bony exposure of the sphenoid and sellar regions is recommended to improve extent of NFPA resection.

Question

Does endoscopic visualization improve visualization of NFPA tumors remaining after standard microsurgery?

Level III Recommendation

Endoscopic approaches are recommended for better visualization of portions of tumors remaining after standard microsurgery, shown in multiple Class III studies in which direct endoscopic visualization revealed residual tumor tissue after initial microsurgery.

Question

Is a surgical strategy of combined transsphenoidal and transcranial approaches useful in NFPA surgery?

Level III Recommendation

For select, invasive NFPAs with significant suprasellar, frontal, and/or temporal extension, the combined surgical strategy of transsphenoidal and transcranial approaches is recommended.

Question

Does use of intraoperative magnetic resonance imaging (MRI) technology improve gross total resection of NFPAs?

Level III Recommendation

Although intraoperative MRI (low-field or high-field) helps improve immediate overall gross total resection of nonfunctioning pituitary adenomas, intraoperative MRI for estimating residual tumor is not recommended due to a reported variable false-positive rate. This false-positive rate may contribute to the higher rate of gross total resection occurring with intraoperative MRI (but at the cost of removing normal tissue) and underscores the importance of incorporating surgical experience in the interpretation of intraoperative MR imaging for surgical decision-making.

Question

Is stereotactic neuronavigation a useful adjunct for NFPA surgery?

Recommendation

There is insufficient evidence to recommend the use of neuronavigation as a useful adjunct for NFPA transsphenoidal surgery.

Question

Does introduction of intrathecal saline or air improve resection of suprasellar NFPAs?

Recommendation

There is insufficient evidence to recommend the use of intrathecal saline or air introduction for suprasellar tumor delivery to augment NFPA resection.

Question

Does perioperative cerebrospinal fluid (CSF) diversion decrease the risk of postoperative CSF leak for NFPA surgeries?

Recommendation

There is insufficient evidence to recommend the use of perioperative CSF diversion to prevent postoperative CSF leak.

Question

Is there a superior dural closure technique to prevent CSF leaks?

Recommendation

There is insufficient evidence to recommend the use of specific dural closure techniques to prevent postoperative CSF leak for NFPA resection.

Definitions

Evidence Classification for Therapeutic Studies

Class I	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II	Evidence provided by well-designed observational studies with concurrent controls (e.g. case control and cohort studies)
Class III	Evidence provided by expert opinion, case series, case reports and studies with historical controls

Evidence Classification for Diagnostic Studies

Class I	Evidence provided by one or more well-designed clinical studies of a <i>diverse</i> population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios
Class II	Evidence provided by one or more well-designed clinical studies of a <i>restricted</i> population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios
Class III	Evidence provided by expert opinion or studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios

Strength of Recommendations Rating Scheme

Level I: High degree of clinical certainty (Class I evidence or overwhelming Class II evidence)

Level II: Clinical certainty (Class II evidence or a strong consensus of Class III evidence)

Level III: Clinical uncertainty (inconclusive or conflicting evidence or opinion)

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Nonfunctioning pituitary adenoma (NFPA)

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Treatment

Clinical Specialty

Endocrinology

Geriatrics

Neurological Surgery

Neurology

Oncology

Radiation Oncology

Radiology

Intended Users

Physicians

Guideline Objective(s)

To survey the literature for evidence-based guideline recommendations concerning the surgical approaches of transsphenoidal microsurgery, endoscopic resection, and transcranial surgery, as well as adjunctive technological innovations such as intraoperative magnetic resonance imaging (MRI) and neuronavigation, plus technical concerns of cerebrospinal fluid (CSF) diversion and dural closure

Target Population

Adult patients with nonfunctioning pituitary adenomas (NFPAs) undergoing initial operative treatment

Interventions and Practices Considered

1. Transsphenoidal microsurgery or endoscopic resection
2. Use of transsphenoidal approach in elderly patients
3. Adequate bony exposure of the sphenoid and sellar regions
4. Endoscopic approaches for better visualization of portions of tumors remaining after standard microsurgery
5. Combined surgical strategy of transsphenoidal and transcranial approaches

Note: Intraoperative magnetic resonance imaging (MRI) for estimating residual tumor (was considered but not recommended). The following practices were considered but not recommended because of insufficient evidence: use of neuronavigation as an adjunct for nonfunctioning pituitary adenoma (NFPA) transsphenoidal surgery, introduction of intrathecal saline or air for suprasellar tumor delivery to augment NFPA resection, use of perioperative cerebrospinal fluid (CSF) diversion to prevent postoperative CSF leak, and specific dural closure techniques to prevent postoperative CSF leak.

Major Outcomes Considered

- Gross total resection rate
- Residual/recurrent tumor rate
- Symptom relief
- Operative time
- Complications of surgery
- Mortality

Methodology

Methods Used to Collect/Select the Evidence

METHODS USED TO COLLECT/SELECT THE EVIDENCE

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

General Search Strategy

Literature Search

The guideline task force collaborated with a medical librarian to search for articles published from January 1, 1966, to October 1, 2014. Searches were conducted in two electronic databases, PubMed and The Cochrane Central Register of Controlled Trials. Strategies for searching electronic databases were constructed by the guideline task force members and medical/research librarians using previously published search strategies to identify relevant studies. The root search strategies are provided in Appendix A of the introduction and methodology companion and the chapter-specific search strategies are provided in the appendix of the full version of the guideline (see the "Availability of Companion Documents" field).

The searches of electronic databases were supplemented with manual screening of the bibliographies of all retrieved publications. The bibliographies of recent systematic reviews and other review articles for potentially relevant citations were also screened. All articles identified were subject to the study selection criteria listed below. The guideline task force also examines lists of included and excluded studies for errors and omissions.

Article Inclusion Criteria

Articles were retrieved and included only if they met specific inclusion criteria. These criteria were also applied to articles provided by the evidence-based clinical practice guideline task force members who supplemented the electronic database searches with manual searches of the bibliographies. To reduce bias, these criteria were specified *a priori* before conducting the literature searches. For the purposes of this guideline, articles had to meet the following criteria to be included as evidence to support the recommendations presented in this guideline:

- Investigated patients suspected of having a pituitary mass
- Enrolled patients ≥ 18 years of age
- Either enrolled exclusively nonfunctioning pituitary adenoma (NFPAs) patients OR combined the results of patients with NFPAs and functioning pituitary adenomas and/or other pituitary masses with $\geq 90\%$ of the patients having NFPAs
- Was a full article report of a clinical study
- If a prospective case series, reported baseline values
- Appeared in a peer-reviewed publication
- Enrolled ≥ 10 NFPA patients per arm per intervention (20 total) for each outcome
- Was of humans
- Was published in or after 1966
- Quantitatively presented results

Article Exclusion Criteria

Articles of the following types were excluded as evidence to support the recommendations presented in this guideline:

- In vitro studies
- Studies performed on cadavers
- Studies not published in English
- Medical records reviews, meeting abstracts, historical articles, editorial, letters, or commentaries
- Systematic reviews, meta-analyses, or guidelines developed by others

Specific Methods for This Guideline

Literature Search

The task force collaborated with a medical librarian to search for articles published from January, 1, 1966, to October 1, 2014. Authors searched 2 electronic databases, PubMed and The Cochrane Central Register of Controlled Trials. Strategies for searching electronic databases were

constructed by the evidence-based clinical practice guideline taskforce members and the medical librarian using previously published search strategies to identify relevant studies (see Appendix A in the full guideline).

Results

The medical literature was searched using search terms encompassing surgical resection strategies specific to transsphenoidal and intraoperative magnetic resonance imaging (MRI) techniques. Abstracts from the results of these searches were screened, and full-text articles from potentially significant articles were reviewed.

Articles found on literature review based on the above criteria include 35 Class III studies involving transsphenoidal microscopic surgery, 20 Class III studies for endoscopic surgery, and 9 Class III studies involving transcranial surgery for NFPA resection. Studies that included results from multiple or combined surgical approaches were included in several of the above categories. For this guideline, transsphenoidal surgery is a broad term that includes both microscopic and endoscopic approaches. Specifically, microscopic transsphenoidal surgery or transsphenoidal microsurgery refer to surgeries performed with microscope visualization and tumor resection via either sublabial or endonasal pathways, whereas endoscopic transsphenoidal surgery refers to using endoscope visualization and resection via various anatomical corridors (usually variations of the endonasal and endosinus corridors); the transcranial approach consists of supratentorial craniotomy microscopic tumor resections.

Number of Source Documents

A total of 56 articles were included as evidence.

A flow chart summarizing study selection can be found in Figure 1 of the full version of the guideline (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification for Therapeutic Studies

Class I	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
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Class III	Evidence provided by expert opinion or studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Rating the Quality of the Evidence and Levels of Recommendations

The quality and classification of evidence (see the "Rating Scheme for the Strength of the Evidence" field) was rated using an evidence hierarchy developed by the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Guidelines Committee for each of four different study types: therapeutic, prognostic, diagnostic, and economic or decision modeling. The methodology used to conduct quality evaluations of the evidence can be located on the [CNS Web site](#) (see also the "Availability of Companion Documents" field). The level/strength of recommendation (i.e., Level I, II, or III) was linked to the quality of the overall body of evidence included in the chapter and in support of a given recommendation.

Methods Used to Formulate the Recommendations

Expert Consensus (Nominal Group Technique)

Description of Methods Used to Formulate the Recommendations

Process Overview

A multidisciplinary task force comprised of physician volunteers and evidence-based medicine trained methodologists conducted a systematic review of the literature relevant to the management of non-functioning pituitary adenomas (NFPAs). The physician volunteers represented neurosurgeons, neuro-ophthalmologists, neuroradiologists, and endocrinologists with expertise in pituitary adenomas. The evidence-based medicine trained methodologists had previous experience in guidelines production for the Joint Guidelines Committee (JGC) of the Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS). During the development process, the task force participated in a series of conference calls and meetings. Multiple iterations of written review were conducted by the individuals of the panel and various CNS/AANS Committees prior to approval.

Guideline Task Force Panel Consensus

The guideline task force panel included context experts from multiple disciplines and various areas of therapy to address the topics addressed in this guideline. Sub-task force members were assigned to a specific chapter and were involved in the literature review, the creation and editing of the evidence tables, reviewing and voting of the final recommendations.

Voting on the Recommendations

The task force used a structured voting technique to finalize and approve the final recommendations, language, and strength of recommendations, presented in this review. The voting technique is referred to as the nominal group technique. This technique includes up to three rounds of voting, using secret ballots to ensure task force members are blinded to the responses of other task force members. All the recommendations in this review were approved following the first round of voting and no further discussion was needed to finalize the recommendations. During the course of editing and finalization of the document, changes were made to allow recommendations to conform to the rules of evidence and language as described above. When this occurred, the changes were reviewed and approved by the group.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations Rating Scheme

Level I: High degree of clinical certainty (Class I evidence or overwhelming Class II evidence)

Level II: Clinical certainty (Class II evidence or a strong consensus of Class III evidence)

Level III: Clinical uncertainty (inconclusive or conflicting evidence or opinion)

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Guideline Approval Process

The guideline draft was circulated to the entire task force for final review and approval prior to submission for peer review by the Joint Guidelines Committee (JGC) of the Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS). Due to the reviewers' knowledge of evidence-based medicine and clinical practice guidelines methodology training, the JGC peer reviewers served as the journal's editorial reviewers. As a part of the JGC review process, the reviewers provided input on the content of the guideline and suggested revisions prior to approval and endorsement of the draft guideline by the CNS and AANS prior to publication. The development of this guideline was editorially independent from the funding agencies (CNS Executive Committee, and AANS/CNS Joint Tumor Section Executive Committee), the CNS and Joint Tumor Section.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

All of the evidence consisted of Class III studies.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Both endoscopic and microscopic transsphenoidal approaches show postoperative symptom relief in patients with nonfunctioning pituitary adenomas (NFPAs), with the extent of tumor resection improved by adequate bony exposure and endoscopic visualization.

Potential Harms

- In one study, complications of transsphenoidal microsurgery included 24% postoperative hypopituitarism and 1 death due to hemorrhage. Another study reported 3% surgically related mortality, 1% cerebrospinal fluid (CSF) leak, and 2% need for permanent CSF shunting. A third study reported postoperative complications of diabetes insipidus (14%), CSF leak (5%) and 13% required subsequent trans-cranial craniotomy to completely remove tumor.
- Tumor size and cavernous sinus invasion are factors that adversely impact the rate of gross total resection of NFPAs for all surgical approaches.
- In elderly patients (greater than 64 years old) perioperative complications were higher in the transcranial group (5 of 6 patients) compared to the transsphenoidal group (6 of 32 patients).
- A study with combined transsphenoidal and transcranial resections reported complications of transient oculomotor palsy, mild hemiparesis, and postoperative seizures.

Refer to the full version of the guideline (see the "Availability of Companion Documents" field) for additional discussion of complication rates for the various surgical approaches in reported studies.

Qualifying Statements

Qualifying Statements

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a physician volunteer task force as an educational tool that reflects the current state of knowledge at the time of completion. The presentations are designed to provide an accurate review of the subject matter covered. This guideline is disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in its development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a physician should be sought. The recommendations contained in this guideline may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in this guideline must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Kuo JS, Barkhoudarian G, Farrell CJ, Bodach ME, Tumialan LM, Oyesiku NM, Litvack Z, Zada G, Patil CG, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on surgical techniques and technologies for the management of patients with nonfunctioning pituitary adenomas. *Neurosurgery*. 2016 Oct;79(4):E536-8. [44 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Oct

Guideline Developer(s)

Congress of Neurological Surgeons - Professional Association

Source(s) of Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the Tumor Section of the Congress of Neurological Surgeons and the American Association of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

Guideline Committee

Nonfunctioning Pituitary Adenoma Guideline Task Force

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Potential Conflicts of Interest

All Nonfunctioning Pituitary Adenoma (NFPA) Guideline Task Force members were required to disclose all potential conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Joint Guidelines Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of Task Force Members with possible conflicts and restrict the writing, reviewing and/or voting privileges of that person to topics that are unrelated to the possible COIs.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

Guideline Endorser(s)

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [Neurosurgery Web site](#) . Also available in ePub format from the [Neurosurgery Web site](#) .

Availability of Companion Documents

The following are available:

- Kuo JS, Barkhoudarian G, Farrell CJ, Bodach ME, Tumialan LM, Oyesiku NM, Litvack Z, Zada G, Patil CG, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on surgical techniques and technologies for the management of patients with nonfunctioning pituitary adenomas. Full guideline. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2016 Oct. 50 p. Available from the [Congress of Neurological Surgeons \(CNS\) Web site](#) .
- Aghi MK, Chen CC, Fleseriu M, Newman SA, Lucas JW, Kuo JS, Barkhoudarian G, Farrell CJ, Sheehan J, Ziu M, Dunn IF. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the management of patients with nonfunctioning pituitary adenomas: executive summary. Neurosurgery. 2016 Oct;79(4):521-3. Available from the [Neurosurgery Web site](#).
- Aghi MK, Bodach ME, Tumialan LM, Oyesiku NM, Patil CG, Litvack Z, Zada G. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the management of patients with nonfunctioning pituitary adenomas: introduction and methodology. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2016 Oct. 12 p. Available from the [CNS Web site](#) .
- Congress of Neurological Surgeons (CNS). Guideline development methodology: endorsed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the AANS/CNS Joint Guideline Committee. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2012 Feb. 12 p. Available from the [CNS Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 10, 2017. The information was verified by the guideline developer on February 22, 2017.

Copyright Statement

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